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ABSTRACT

Reviewed in the report is research on hyperkinesis, specifically B. Feingold's hypotheses on the role of salicylates and food additives. Criticisms of Feingold's studies are seen to include methodological weaknesses (no double blind controlled experiments), nutritional concerns over the adequacy of prescribed diets, and lack of a specifically focused hypothesis. Guidelines for experimental design are offered, and ethical considerations in future studies are discussed. (CI)

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THE NATIONAL ADVISORY COMMITTEE ON HYPERKINESIS AND FOOD ADDITIVES

REPORT TO THE NUTRITION FOUNDATION

June 1, 1975

EC 092405

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Introduction

Aware of the anxiety created by the publicized hypothesis advanced by Dr. Ben F. Feingold (1) in 1973 implicating many widely distributed or highly nutritious food-stuffs and undesignated food additives as potential factors in hyperkinesis, The Nutrition Foundation has supported a responsible, critical review by a competent group of expert medical and behavioral scientists of evidence relative to this hypothesis. The scientists who comprised the review committee were selected and identified by the offices of major scientific and medical organizations: American Medical Association's Council on Foods and Nutrition; American Psychiatric Association; American Association of Child Psychiatry; Society of Toxicology; Council for Exceptional Children; American Alliance for Health, Physical Education; Institute of Food Technologists; American Society for Clinical Nutrition; American Dietetic Association; The National Nutrition Consortium; Life Sciences Research Office of the Federation of American Societies for Experimental Biology; Committee on Nutrition of the American Academy of Pediatrics; and the Food and Nutrition Board of the National Academy of Sciences.

An intensive literature search seeking all relevant published information was conducted and copies of the published materials were provided each member of the Committee. The published materials were supplemented with manuscripts of talks, research proposals, or other pertinent unpublished information obtainable from any of the participating sources. Immediately prior to the initial meeting of the Committee, the book by Dr. Ben F. Feingold entitled *Why Your Child Is Hyperactive* was published (2) and copies were made available to the conferees attending the first Committee meeting.

The Committee was charged with the responsibility to (a) review critically and objectively the nature of evidence relative to the hypothesized relationship, (b) recommend whether additional investigations were justified or desirable, and, if so, (c) provide guidelines for the

experimental design of appropriate studies which would result in obtaining valid data upon which conclusions might be formulated. The background of the committee is such as to provide valuable guidance in assessing evidence and design of any subsequently projected clinical and experimental investigations of the postulated relationship between hyperkinesis and food.

Dr. Morris Lipton, Professor of Psychiatry, University of North Carolina and a member of the American Psychiatric Association was elected Chairman.

An initial meeting was held January 12-14, 1975, at Harrison House in Glen Cove, Long Island. Observer representatives were invited from the Food and Drug Administration, the Ford Foundation, Grocery Manufacturers of America, Inc., National Institute of Education, the National Institutes of Health and from three major food companies. The identity of these observers and their affiliations are listed in the Appendix. The observer from the National Institutes of Health was unable to attend this initial meeting, but has been provided with information exchanged prior and subsequent to the meeting.

Resource personnel were invited who could provide background information, who were knowledgeable concerning or involved in current investigations or were planning research in the area. These included:

Dr. GERALD A. GLEICH, Allergist
The Mayo Clinic
Rochester, Minnesota

Dr. DONALD K. ROUTH, Research Psychologist
Child Development Research Center
University of North Carolina
Chapel Hill, North Carolina

Dr. BEN F. FEINGOLD, Retired Staff Member
Kaiser-Permanente Medical Center
San Francisco, California

and medical and behavioral scientists involved in research and planning of studies at the following centers:

University of Wisconsin:

DR. PETER EICHMAN
Professor of Neurology
Neurological Institute
Madison, Wisconsin

DR. PRESTON HARLEY
Department of Neurology
University of Wisconsin Medical Center
Madison, Wisconsin

University of Pittsburgh:

DR. CHARLES GOYETTE
Project Coordinator
Western Psychiatric Institute and Clinic
Pittsburgh, Pennsylvania

Harvard University:

DR. GEORGE KERR
Associate Professor
Department of Nutrition
Harvard School of Public Health
Boston, Massachusetts

University of Minnesota:

DR. MICHAEL APPLEMAN
Department of Education
St. Paul, Minnesota

Resource personnel, as well as members of the Advisory Committee, presented relevant background reviews which were followed by free discussion and exchange participated in by all persons in attendance at the meeting. The background discussions pertained to the broad areas of the nature of hyperkinesis; methods of assessing its severity and the effectiveness of therapy; an extended discussion by Dr. Feingold concerning his hypothesis and management regimen; a basic discourse on modern understanding of and new methodology for identifying types of allergenic responses and food allergies; an interim report of data on eight patients observed in the Conners-Goyette study from the University of Pittsburgh; clinical observations and protocols under development; investigations at the University of Utah; protocols of studies projected at the University of Wisconsin, Harvard University and in Minnesota. Studies in two experimental animal models were presented and their potential usefulness as screening or evaluation techniques discussed. Against this background, members of the Advisory Committee have reviewed and further assessed a variety of points identified during the workshop. This report summarizes the present views of the Advisory Committee and indicates its recommendations for further studies.

The Nature of Hyperkinesis

The terms "hyperactivity, hyperkinesis and hyperkinetic syndrome" have been loosely employed in both lay and professional writings. Strictly speaking, hyperactivity is one of the symptoms of the hyperkinetic syndrome. Frequently, the latter term is mistakenly used interchangeably with that of the syndrome of "minimal brain dysfunction," which syndrome is of itself ill-defined. Indeed, Strother (3) has opined that "greater attention should be paid to classifying the very heterogeneous group of children now included under this rubric into more specific and homogeneous categories." There is no agreement—and little good evidence—as to the extent to which several seemingly related syndromes overlap. Definitive separation of these conditions has not been made in the writings of most physicians, behavioral scientists, or educators, including Dr. Feingold.

In an effort to clarify "the murky realm of nosology" P. H. Wender (4) notes that there is evidence for several etiological subgroups, and that the "hyperkinetic behavior syndrome" includes a number of clinical features: hyperactivity; short attention span and poor powers of concentration; impulsivity and the inability to delay gratification. There is diminished ability to experience pleasure and frequent refractoriness to disciplinary measures of any sort. Variably affected are perceptual-cognitive functions and neurologic function and coordination. These problems produce significant school underachievement in most children with the disorder. In school it contributes to classroom disruption; at home it is disruptive to family relations. Estimates of its incidence in U.S. schools range widely, frequently from 3 to 10%. Feingold (1) quotes some estimates as high as 25% or more of all children in certain schools. Others estimate a similar percentage of children as receiving drugs for the disorder (5). These variations reflect the inappropriate equating of different conditions "under the rubric of learning disabilities (i.e., hyperkinesis and reading retardation)" as well as other influences (6).

The origin and development of the disorders have not been established. Indeed, it is not even certain whether this is a discreet illness or a syndrome of many causes. There is evidence to support the hypothesis that some minimal brain dysfunction is genetically determined, produced

by subtle central nervous dysfunction of biochemical nature (4). It is also hypothesized that some minimal brain damage may result from intrauterine factors or from difficult birth process (7). In rare instances low level lead encephalopathy may contribute to such a syndrome, if one can extrapolate from experimental animal models (8, 9).

The lack of clarity in regard to these conditions is emphasized by the statement of The Council on Child Health of the American Academy of Pediatrics (10):

> "One must be cognizant of the fact that there is probably more confusion in relation to diagnosis and appropriate criteria for the use of medication for the treatment of hyperkinetic children than there is regarding the actual medication. Many physicians, as well as the general public, do not truly appreciate the differential diagnosis of the overactive child. It may be the result of basic personality, anxiety, subclinical seizure disorders, strictly in the eyes of the beholder, or true hyperkinesis; the latter is the only condition in which stimulants might be expected to be beneficial."

The Council on Child Health of the American Academy of Pediatrics (10) further notes that:

> "The hyperkinetic child is typically one of normal intelligence who fails to learn at a normal rate even though he is given the same educational opportunities as children with equal intelligence. He usually exhibits to some degree (1) short attention span, (2) easy distractibility, (3) impulsive behavior, and (4) overactivity. Although other behaviors ofttimes are seen in children with normal intelligence and academic lag, stimulant drugs seem to be most effective in the four behaviors just mentioned. Little is known about the effect of stimulant drugs on such things as poor motor integration, deficits in the perception of space, form, movement and time, and disorders of language or symbol development."

Response to drug therapy is unequivocal when it occurs and after satisfactory response to short term treatment, omission of the drug is immediately evident to those around the child, because he rapidly returns to the base line abnormal behavior (10). After long periods of control, discontinuance of drug therapy may be followed by remission in some 25% of patients. It is the practice of "many clinicians [to] discontinue the use of medication over each long school vacation; this

allows the child to start a new year without medication. The medication is resumed only if the syndrome that initiated the original treatment hinders satisfactory school progress" (10).

There is little reliable information about the prognosis or natural course of hyperkinesis, how long the average child may benefit from medication, or whether taking stimulant drugs alters the ultimate prognosis in a substantial way. As an example, in a study recently published (11) in JAMA, data were summarized on 42 children, 13 of whom had been followed for two years, and 29 for one year. The subjects had been part of a double blind placebo study on the effect of different dose levels of Ritalin on behavior and school performance and were tested at one month intervals. Thus the population employed were known to be Ritalin responsive.

Twenty-six per cent of those taken off medication exhibited no deterioration of performance. This observation is important to interpretation of any studies of the effect of newly instituted regimens because the previously occurring symptoms do not always return immediately when medication is discontinued.

In a study at the University of North Carolina designed quantitatively to measure the motor activity and interest span of children diagnosed as hyperkinetic, Dr. Routh (12) reported that of 78 referrals from physicians, teachers and parents, 47% of the children were judged to be overactive and 53% were not. This, despite the fact that all of the children were considered to be "problem children" by those referring them to the testing service. Difficulties are inherent in all measurement techniques. Behavior perceived as hyperactivity may be more accurately described as non-goal directed activity. There is a sub-group of children with many of the other characteristics of minimal brain dysfunction who are in fact hypoactive.

Examples are numerous to illustrate the inconsistencies in rating of a child's activity by observers with different relationships to the subject, i.e., mothers, fathers, teachers, physicians, independent observers. Differences in perception by the observer do not follow a consistent pattern determined by the relationship to the child. For example, in a study in Iowa of teacher ratings of hyperactivity, it was found that older age teachers rated more children hyperactive than did young teachers (13).

Clinical experience indicates that many factors alter the activity patterns of such children or the perception of them by parents. Such factors range from the presence or absence of breakfast, weather conditions and resultant seasonal cycles that alter activities during cold seasons, to the interpersonal family relationships or existence of disruptive family problems. Age of the child appears to be another determinant of detection of the syndrome of hyperactivity. The majority of cases are noted at about the age of entry to school and there usually is a gradual diminution in the hyperactivity approximately at puberty or slightly

thereafter. While some observers cite isolated cases of identifiable hyperkinesis in older individuals, this not the usual pattern. The syndrome is not recognized as a problem by school authorities in some areas of the world—again an example of differences in perception or of occurrence.

The diagnosis of hyperkinesis depends primarily upon the trained clinician's judgment based upon history and observation of behavior. Some studies have employed trained classroom observers to help confirm the diagnosis. Again, behaviors which can be objectively measured may not adequately reflect the kind of problems that different children have. Objective measures of attention span have been developed (usually continuous performance tasks) and have been employed in making the diagnosis in some studies. Standard questionnaires completed by parents and teachers and involving observations at several different points in time provide useful evaluatory techniques.

The Feingold Hypothesis

In June 1973, Dr. Ben Feingold, a pediatric allergist from San Francisco, orally presented a preliminary report (14) in which he stated that hyperkinesis was associated with the ingestion of salicylates, of compounds which cross-reacted in the body with salicylates, and with common food additives.[8] This presentation was followed by a signed editorial in October, 1973 (1). The October 30, 1973 Congressional Record (16) contained the text of a paper given by Dr. Feingold at a meeting in London the month before and an account by a writer for the *Washington Post*. Dr. Feingold's paper printed in the Congressional Record yielded calls for the elimination of "food additives" from school lunch programs. He later restated his position in a book (2) entitled,

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[8] The term "food additive" is of itself a broadly encompassing one which is too often loosely used. The Food Protection Committee of the Food and Nutrition Board, National Academy of Sciences-National Research Council defines food additives (15) as "a substance or a mixture of substances, other than a basic foodstuff, that is present in a food as a result of any aspect of production, processing, storage or packaging. The term does not include chance contaminants." It does embrace such diverse substances as many essential nutrients (vitamins, minerals), flavoring agents (naturally occurring or synthetic), functional ingredients, preservatives and antioxidants (naturally occurring or synthetic), etc.

The U.S. Food and Drug Administration has defined "food additive" as: "any substance the intended use of which results or may reasonably be expected to result, directly or indirectly, in its becoming a component or otherwise affecting the characteristics of any food (including any substance intended for use in producing, manufacturing, packing, processing, preparing, treating, packaging, transporting, or

Why Your Child is Hyperactive. This book not only advocates the hypothesis, but also describes his dietary method of treatment. The presentation and the publication of the book have attracted a great deal of publicity. It has resulted in hundreds of letters to pediatricians, especially from parents seeking assistance, and although Dr. Feingold advocates his diet under medical management, it probably will lead to self-treatment programs.

Dr. Feingold currently advocates that a special label, identifying foods "without additives," be made available to be placed on all foods sold to the American public. By implication, of course, foods not so labeled would be considered by the interested consumer to contain "synthetic" additives.*

Dr. Feingold has not presented a specifically focused hypothesis. He depends upon the empirical observations he has made with patients under his therapeutic regime and on his special diet. He has reported that his management regime and an elimination diet (the Kaiser-Permanente or K-P diet), which was designed to be low in salicylates and free of "food additives," effectively treats 48% of the children presented to him with hyperkinesis. Of the children who respond, under his guidance, about ⅔ do so dramatically; the other third "favorably." It is important to note that Dr. Feingold claims (2) a response in *only half* of the children treated and dramatic response in but ⅔ of these. Thus his percentage of success is of the same magnitude that occurs following cessation of drug therapy (11).

Although Dr. Feingold's claims may prove valid, and, if so, may represent a major breakthrough in the treatment of this complex condition, the fact remains that his hypothesis is subject to serious criticism on several grounds. Of especially critical significance is the fact that no double blind controlled experiments have been conducted which permit the conclusion that dietary constituents are the critical variables. His observations, therefore, have served as a basis for generating an hypothesis, but they are inadequate for rigorous testing of the hypothesis. They do not justify definitive conclusions.

holding food; and including any source of radiation intended for such use), if such substance is not generally recognized, among experts qualified by scientific training and experience to evaluate its safety, as having been adequately shown through scientific procedures (or, in the case of a substance used in food prior to January 1, 1958, through either scientific procedures or experience based on common use in food) to be safe under the conditions of its intended use."

The distinction between "naturally occurring" and "synthetic" is usually vague and often relates to origin, not identity of the compound or mixture. For example, chemically synthesized β-carotene, the precursor of vitamin A, is "synthetic" while the chemically identical material biologically present in the carrot is "natural." Similarly, a mixture of three or so synthetic chemical components of a natural flavoring agent is termed "synthetic," while the "natural" agent contains these same components plus an additional number of compounds. Thus, the separation into "natural" and "synthetic" *per se* has no biological significance.

According to the Feingold regimen, not only the children, but their entire families are placed on the diet and regimen in order to ensure compliance. Parents are instructed to spend Saturday mornings making additive-free candy and cake with their children. There can be no question but that the total regimen significantly alters the structure and dynamics of the families by the introduction of the diet and its restrictions upon the child and his family. Since in many children hyperactive behavior is associated with family problems, it is quite possible that the alterations in the family dynamics may be causally related to the reported improvement in the child. Second, hyperactive behavior and its rating on a severity score are both subject to suggestibility. Dr. Feingold is charismatic and certain of the value of his program. It is possible that the confident expectations generated in the patient and the family affects the syndrome itself, or at least the parents' ratings of the altered severity of the behavioral pattern. Third, parents or teachers who rate the children know that they are on the diet and this knowledge may influence their ratings. Fourth, objective rating scales like that developed by Dr. Keith Conners (17) have not been systematically employed to measure the parameters of the disorder or improvement. Dr. Feingold's improvement ratings are global, not specific.

The exact additive and nutrient content of the Feingold elimination diet remains difficult to assess. The proscriptions invoked may eliminate important and as yet unidentified food constituents. Knowledge of the chemical composition of foodstuffs is fragmentary. A number of common sources of important nutrients are proscribed, making it especially important that careful planning and food selection pertain to assure that nutrient requirements are met for any long term period of restriction to the regimen. Development of information on nutrients supplied by the regimen are currently underway in order to evaluate dietary patterns under the restrictions imposed and to determine if they may meet the long term nutrient needs of children. Until this question is answered, the committee feels that this regimen should not be used without competent medical supervision.

The initial rationale of the elimination diet advocated by Dr. Feingold was to avoid salicylate and salicylate-like compounds which occur naturally or as a result of processing. Data upon the naturally occurring salicylate compounds are notably incomplete and the dietary plan is based upon studies utilizing old and less-than-definitive methodology. The K-P diet calls for elimination of many commonly eaten members of the widest variety of food classes, with and without food additives, of all categories. There is *no* identifiable single substance or group of substances which the diet specifically removes and to the absence of which any observed effect might be attributed. The validity of this assessment by the Committee is indicated by Dr. Feingold's shift of emphasis from a suspected role of salicylates, aspirin-like compounds, to other food ingredients. It is noteworthy also that the K-P regimen (2)

proscribes a wide variety of sundry items including over-the-counter medications, toothpastes and tooth powder, mouthwashes, cough drops, throat lozenges, antacid tablets and perfumes. Accordingly, the regimen markedly modifies other ingestibles as well as food.

A review (*18*) of the preliminary studies on eight patients by the Pittsburgh group studied in relation to the K-P regimen revealed that the majority of those subjects were judged by the parents to have exhibited improvement, sometimes continuously, regardless of which of two dietary regimens (the K-P diet or a "control") they were following. There were discrepancies, however, between the assessment by parents and by teachers of perceived behavioral changes in a portion of the studies and the teacher assessment was absent in a considerable number of the observational periods reported. Although the data were inconclusive, the preliminary results of the pilot studies were consistent with an interpretation of placebo effects and of variations in perception on the part of different observers, both of which are known to occur in studies of hyperkinesis.

Summary

The Committee concludes that data from critically designed and executed studies, free of the deficiencies of design noted, must be available before firm conclusions can be reached on the Feingold hypothesis. Accordingly, the Committee has considered at length the experimental design characteristics necessary to obtain definitive, interpretable data which may permit a decisive interpretation.

Guidelines for Experimental Design

While a variable number of experimental approaches may contribute to resolution of these complex questions, certain approaches will be more informative and feasible than others. The possibility of producing a wide variety of dietary products in identical pairs containing, or free of, specific chemical ingredients and indistinguishable to the consumer was considered. To execute effectively a program utilizing many such foods and to maintain the regimen as a complete double blind study would involve an enormous expenditure. On the other hand, the utilization of alternate dietary plans, i.e., the K-P diet and a "control," even when randomly administered, precludes strict double blind testing and introduces the variable placebo effect.

Patient compliance is difficult to control and monitor and might most easily be assured in a totally institutional or residential population. Potential methods for controlling compliance might be detection of metabolites or a marker in urine. But committee members are doubtful that appropriate technology may be available for such monitoring. This is being explored.

In order adequately to test the Feingoid hypothesis, it is desirable that an "exclusion" diet planned for nutritional adequacy and in keeping with the K-P proscriptions be designed and utilized. Strong preference was expressed by the Committee that in a home setting there be used but one diet, i.e., no "control diets," because of anticipated difficulties in assuring compliance and the impossibility of avoiding the placebo effect. The use of a control diet would be more acceptable in a residential or institutional setting.

In any study it is essential to establish a valid behavioral base line before any manipulation is tried. The multiple and manifold nature of symptoms make it mandatory that the base line be established by having more than a single point and a *minimum* of two observations are required. The observations and evalaations should include assessments by the same observers in at least two different points in time and the observers should be the same as those who will subsequently assess the patient's behavioral pattern during the remainder of the study.

It was agreed that, after establishment of the behavioral base line and institution of the dietary regimen, a well designed double blind study utilizing, as a test or challenge, conventional foods prepared to be free of, or to contain, a single challenge ingredient or group of ingredients, would be most informative. The "challenge foods" should be made available for daily consumption by all members of the family. Such foods are more acceptable than capsules and the Committee recommends that at least two forms be developed. Each of these forms should be prepared in separate lots, one free of challenge material and another containing the challenge substance(s). They should be packaged in such manner as to preserve the double blind nature of the observations. Sequentially identified individual units should be packaged for consumption by the family, utilizing randomization and an unindicated code.

Behavioral observations of subjects will be made throughout the course of the experiment and only upon conclusion of individual studies will the challenge code be broken. In the event of adverse somatic reactions or deterioration of behavior, of course, the eating of the "challenge food" may be interdicted. A direct comparison of observed behavioral patterns with consumption or non-consumption of the "challenge substance" will permit definitive conclusions. These studies demand adequate independent monitoring and an appropriate number of participating families with hyperkinetic children.

The Committee emphasizes the necessity for utilization of quanti-

tative base line measurements of behavior and of behavioral changes. As a minimum it is agreed that the Conners scale should be adopted and that assessments should be made by the use of independent (non-parent, non-teacher) classroom observers (such as graduate students in psychology) as well as by teachers and parents. In addition, there should be a clinical assessment by a physician at the beginning of the experiment and at least at monthly intervals throughout and additional measurements as feasible within the resources of the research team.

At least two weeks of base line data are recommended, the exact circumstances of which will depend upon the prior treatment (medication, diet or none), if any, of the patient. The frequency and quantity of observations during the base line period and the experimental periods should be such as to assure adequate assessment of individual variations. The reliability of all observations, including the initial observation, should be maximized by having the same observers rate the child throughout. Because of the known effect of medication on the symptoms being observed, the Committee felt that whenever possible any study should include a significant preliminary period of approximately two weeks during which there is no medication. It was agreed it would be advisable for at least one study to evaluate children who had never received drug medication. The period of observation following the base line should be a minimum of one month for the diet.

The code for the challenge materials should not be broken until the study is completed and the behavioral data are available for direct comparison with the data on the consumption of the challenge or control food. The advantage of the proposed approach is that interdiction is possible at any point simply by stopping the "challenge food." Careful records should be maintained of all such instances.

Ethical Considerations

The question of ethical acceptability of such studies has been carefully considered and the Committee agrees upon the following points:

The subject and the family will benefit from participation in such experiments whether:

(a) a challenge material can be incriminated, and thereby the opportunity of avoidance of a specific offending material results; or

(b) there is confirmed in a well controlled setting the value of the restricted diet as opposed to other factors; or

(c) no benefit occurs and thereby a troublesome exclusion diet of indefinite duration is avoided.

Interdiction of challenge feeding may occur at any point it is considered to be indicated. Dr. Feingold reports that there is rapid recovery (upon re-establishing his regimen) from the exacerbations that children on his regimen experience upon breaking of compliance.

Experimental Animal Models

Appropriate experimental animal models would seem to offer a potentially useful method for study of the possible relationships of foods and food ingredients to behavioral abnormalities and particularly promising for screening for any such effects. Accordingly, the Committee has reviewed three examples of promising models.

Rats made anoxic at birth with carbon monoxide later manifest hyperkinetic activity (19) which subsequently disappears upon maturation. The phenomenon is similar to that observed in human hyperkinesis.

In other studies, rats receiving low doses of lead during the neonatal period, subsequently develop hyperkinetic activity (9) and these animals respond to drugs in a manner similar to hyperkinetic children. For example, decreased activity occurred when the animals received amphetamine or methylphenidate in contrast to the stimulant effects of these drugs in normal rats. Also, they exhibit increased activity when given sedative doses of phenobarbital. This model system appears to offer a very promising experimental test for the screening of potential therapeutic agents.

Another potential experimental model is the production in developing rats of a syndrome caused by the administration of 6 hydroxy dopamine (6-OHDA) to five day old rat pups (20). This results in destruction of nerve terminals and depletion of brain dopamine to 38% of that of controls. During the first two weeks of post-natal life, the treated pups and littermate controls show little difference in spontaneous movement, but between 2-3 weeks of age, activity dramatically increases, to decline by the 4th week. The altered activity is associated with reduction of brain dopamine concentrations below the level of the normal controls.

These are examples of potential models that offer an opportunity for further study, not only of screening techniques, but also the possibility for elaboration of the mechanism of hyperkinesis.

Needed Funding

The Committee has reviewed funding needed to institute and complete currently projected studies, the protocols of which appear to be most promising of interpretable definitive results. The majority of these

studies are in humans, but the estimates include modest funding for initiation of projects utilizing animal models. The Committee estimates that a total investment of $400,000—$500,000 is required. It is hoped that these funds may be obtained from a number of sources and that their utilization may be coordinated within the framework of the guidelines identified by the Advisory Committee.

Potential sources, in addition to the food and food related industries, logically would appear to be the Food and Drug Administration, National Institute of Education, National Institutes of Health, the National Science Foundation and other foundations. The role of The Nutrition Foundation would appear to be two-fold: a) the continuing support of the Advisory Committee for purposes of assessing and coordinating research program activities and evaluating overall developments and, b) direct support of recommended grants utilizing funds available from a variety of sources. Industry as well as other support for these activities could well be coordinated through administration by The Nutrition Foundation.

The most economical and expeditious initial test of the hypothesis would be to determine, in keeping with the requisite design, the behavioral response to "challenge foods" of known hyperkinetic children currently maintained on the K-P regimen. Dr. Ben Feingold has agreed to cooperate with the Advisory Committee in exploring such an initial study of patients in his series. Other cooperative centers of investigatory work are being explored.

Development of Challenge Food Vehicle

A task force from industry participated in by the staff of The Nutrition Foundation has, during the period beginning from the January 1975 meeting of the Advisory Committee, undertaken the preparation of appropriate challenge and placebo vehicles as recommended by the Advisory Committee. It is anticipated that these coded materials will be ready for utilization by investigators during the spring of 1975.

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Appendix

MEETING OF THE NATIONAL ADVISORY COMMITTEE ON HYPERKINESIS AND FOOD ADDITIVES

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